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LABORATORY PARAMETERS OF ENDOGENOUS INTOXICATION SYNDROME AND LIVER MORPHOLOGY IN CHRONIC HBV-INFECTION

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ABSTRACT

A liver biopsy was studied in 25 patients with chronic viral hepatitis B and a number of morphological changes were revealed: tissue infiltration with lymphocytes, expansion of portal tracts due to fibrosis and moderate lymphocytic infiltration, formation of port-portal septa, stepwise necrosis, hydropic infiltration of hepatocytes, detection of opaque vitreous «hepatocytes and sandy nuclei». As HBV infection progresses, the incidence of diffuse lymphocytic infiltration, the number of port-portal septa, and graded necrosis increases. After antiviral therapy, an improvement in the morphological structure of the liver is recorded. Indicators of endogenous intoxication syndrome have a direct correlation with fibro genesis in HBV infection. In patients with chronic viral hepatitis B who did not receive antiviral drugs, the toxicity index significantly increased and the albumin content decreased in comparison with patients who took antiviral therapy.

KEYWORDS: *Chronic Viral Hepatitis B, Antiviral Therapy, Endogenous Intoxication, Morphology, Index Of Histological Activity, Albumin.*

INTRODUCTION

According to WHO, today there are more than 350 million people with markers of previous HBV infection in the world [10].

Within the framework of traditional concepts adopted in pathology, toxicology, and pharmacology, cell death was considered as a passive degenerative process that occurs as a result of irreversible damage to the cell. The toxic type of cell death is usually referred to as necrosis. Cell death - apoptosis for a long time was considered inherent only in embryonic development and morphogenesis. In most cases of chronic liver damage, including infection with hepatotropic viruses, the main mechanism of cell death is apoptosis [9].

In viral hepatitis, apoptosis can be the result of direct exposure to the virus or mediated by an immune response. Being a universal biological mechanism, apoptosis in viral hepatitis can lead to excessive death of not only hepatocytes, but also other cell populations, reflecting either a systemic immune-inflammatory response to infection or extrahepatic persistence of the virus. Apoptosis of lymphocytes and granulocytes is significantly higher in patients with chronic viral hepatitis B compared with patients with other forms of chronic hepatitis [1].

Liver fibrosis is a local or diffuse increase in the amount of connective tissue, extracellular matrix (collagen fibrous tissue in the perisinusoid space) and the main pathway for the progression of chronic diffuse liver diseases. Cells directly involved in the process of fibrosis are hepatocytes, Kupffer cells, sinusoidal endothelial cells, hepatic stellate cells [2, 4].

The evolution of fibrosis in viral hepatitis is presented as primary fibrosis of the portal tracts with subsequent spread towards the central vein and adjacent portal tracts with the formation of porto-portal and port-central septa [6, 8].

The range of pathological changes in the morphological substrate in viral hepatitis is large. Evidence has been accumulated that patients with chronic hepatitis B are characterized by an increase in angiogenesis indices and a high proliferative activity of Ito cells. Antiviral therapy in patients with hepatitis B leads to positive dynamics of morphological data, accompanied by a decrease in the proliferative activity of Ito cells, a decrease in angiogenesis values and activation of anti-metalloproteinase defense mechanisms. Regression of morphological data during AVT does not depend on the degree of liver fibrosis and the presence of HBeAg before treatment [5, 7].

Endogenous intoxication syndrome is recorded in many pathological conditions of the human body, including viral hepatitis. Cytolysis of hepatocytes with HBV liver damage leads to a decrease in its detoxification and protein synthesizing function, which leads to an increase in the syndrome of endogenous intoxication. The state of the serum albumin molecule, which characterizes its binding capacity, reliably reflects the course of endogenous intoxication syndrome and can be used as a prognosis criterion, the severity of the course and outcome of the disease, as well as the effectiveness of the therapy. The albumin binding reserve index does not depend on the albumin concentration, characterizes only the state of its molecule and is regarded as a marker of intoxication that reliably reflects the status of intoxication of the body. Its

dynamics is reliably associated with the morphofunctional state of the liver. Liver dysfunction leads to an increase in the toxicity index[3, 11].

There are no data in the literature that determine the relationship between the influence of morphological changes in liver tissue on the formation and degree of endogenous intoxication syndrome in chronic viral hepatitis B.

The objective:to determine the nature of histomorphological changes in the liver parenchyma and the severity of the syndrome of endogenous intoxication in patients with chronic viral hepatitis B in the dynamics of the disease and the effect of antiviral therapy on changes in the parameters of the binding capacity of serum albumin.

Materialsandmethods

The study included 25 patients with newly diagnosed chronic viral hepatitis B. Patients were divided into 2 groups. The first group consisted of 11 untreated patients, who underwent NPKP 3 years after the detection of hepatitis B. Patients who formed group I were initially preparing for antiviral therapy, however, for various reasons, they had to postpone therapy to a later date. The second group consisted of 14 people who underwent PFBP 2 years after antiviral therapy.

The patients received antiviral therapy (α-interferon-2a 5 million units daily and entecavir 1,0 g/day). The indications for the appointment of combination antiviral therapy were: positive PCR for HBV DNA, markers of viral hepatitis B in ELISA, increased transaminase levels. The duration of antitherapy was 6 months.

Domestic and foreign test systems were used to determine HBV and HBV DNA markers. All patients underwent percutaneous puncture liver biopsy.

Liver biopsies were obtained by aspiration liver biopsy in patients with chronic viral hepatitis B. Histological examination was performed on paraffin sections. The material was subjected to standard histological processing with the staining of serial sections with hematoxylin, eosin, picrofuchsin according to Van Gieson. We used survey morphological descriptions of structural abnormalities in the liver. In hepatobiopsy specimens, the index of histological activity (IHA) was determined according to Knodell R.G.: 0-3 points - low, 4-8 points - minimal, 9-12 points - moderate, 13-17 points - high activity of hepatitis B.

For light microscopy, the biopsy specimen was fixed with a 10% formalin solution. Paraffin sections were stained with hematoxylin and eosin, picrofuchsin according to Van Gieson.The histological criteria of chronic hepatitis B were assessed: portal tracts, lymphoid follicles in the portal and periportal zones of the hepatic lobule, hydropic and fatty degeneration of hepatocytes, proliferation of interlobular bile ducts, and the presence of port-portal septa.

Statistical analysis of the data obtained was carried out using the Statistica for Windows 6.0 software. Quantitative indicators were compared using the Mann-Whitney method, and qualitative indicators were compared using the Pearson $\chi 2$ test or Fisher's exact method. The equality of the sample means was checked by the Student's t-test. The criterion for statistical significance was $p < 0.05$.

Results of the study

In the first group, 7 patients (63,6%) had a history of acute viral hepatitis B. Distribution by sex: men were 8 patients (72,7%), women - 3 patients (27,3%). Occasional alcohol consumption was noted by 5 patients (45,5%). Morphological changes in liver tissue during primary biopsy in patients of the first group: tissue infiltration with lymphocytes - 100% (diffuse occurred in 5 patients (45,5%), expansion of the portal tracts due to fibrosis and moderate lymphocytic infiltration - in 9 patients (81,8 %). Portal-portal septa - in 9 patients (81,2%), stepwise necrosis - in 10 patients (90,9%). In 6 patients (54,5%), Kaunsilman's little bodies were found, "sandy kernels" were described in 5 patients (45,5%). The average index of histological activity in patients with HBV infection is 8,1 points. The index of albumin tests was 62,6 ± 2,3%, and the toxicity index was 0,62 ± 0,11 (Table 1).

TABLE 1 MORPHOLOGICAL CHARACTERISTICS AND INDICATORS OF THE SYNDROME OF ENDOGENOUS INTOXICATION IN PATIENTS WITH CHRONIC VIRAL HEPATITIS B IN THE DYNAMICS OF THE DISEASE AND TREATMENT (%)

Specifications	First Group (n = 11)	second group (n = 14)	P
Diffuse lymphocyte infiltration of tissue	45,5	21,4	< 0,05
Expansion of portalpaths	81,8	64,3	< 0,05
Stepwise necrosis	90,9	64,3	< 0,05
Portal-portalsepta	81,2	57,1	< 0,05
Tauruscouncilman	54,5	35,7	< 0,05
"Sandcores" ofhepatocytes	45,5	14,3	< 0,001
Average index of histological activity (points)	8,1	4,7	< 0,05
Albuminbindingreserve (%)	62,6±2,3	81,2±3,3	< 0,05
Toxicityindex	0,62±0,11	0,23±0,10	< 0,001

In the second group, among patients with newly diagnosed viral hepatitis B, only 6 patients (42,8%) had epidemiological data on acute viral hepatitis B. By gender, the group included 9 men and 5 women (64,3% and 35,7% respectively).

In the study of hepatobiopsy specimens obtained after antiviral therapy, the following histiostructural changes were revealed: portal tracts in 9 biopsies (64,3%) were slightly enlarged due to fibrosis and moderate lymphocytic infiltration; stepwise necrosis of hepatocytes was observed in 9 patients (64,3%). In 100% of cases (14 patients), there is a single (78,6%) or diffuse (21,4%) lymphocyte infiltration of tissue. Locally, active and inactive port-portal septa were found in 8 patients (57,1%). Nuclear-free acidophilic bodies of Kaunsilman were observed in 5 patients (35,7%). "Sand kernels" are described in 2 patients (14,3%). The average index of histological activity in patients with HBV infection is 4,7 points. The index of albumin tests was 81,2 ± 3,3%, and the toxicity index was 0,23 ± 0,10. The indices of the syndrome of endogenous intoxication in both groups did not reach normal values (both without antiviral therapy and after it), which indicates a disruption of the compensatory capabilities of the liver after a viral lesion, as well as the formation and progression of fibrotic changes in the organ.

CONCLUSION

As HBV infection progresses, there is a change in histiostructural parameters of liver tissue in the form of an increase in diffuse lymphocytic infiltration, an increase in the number of port-portal septa, stepwise necrosis, which is expressed by an increase in the index of histological activity. The use of antiviral therapy leads to a decrease in diffuse infiltration by lymphocytes, a decrease in the number of stepwise necrosis and port-portal septa, a decrease in the expansion of the portal tracts in the hepatobiopsy specimen, as well as the preservation of IGA with a tendency to decrease them. Determination of markers of endogenous intoxication syndrome in patients with chronic viral hepatitis B who have not received antiviral therapy since the detection of HBV infection records a significantly higher toxicity index and a significantly lower albumin binding reserve.

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